# Clinical Experience with Risperidone and Memantine in the Treatment of Huntington's Disease

Eylem Sahin Cankurtaran, MD; Elvan Ozalp, MD; Haldun Soygur, MD; and Aysegul Cakir, MD
*Ankara, Turkey*

We described a 32-year-old woman with Huntington's disease (HD) who presented with severe chorea, psychosis and cognitive abnormalities. We started risperidone at 2 mg p.o./d and increased to 4 mg p.o./d after six weeks. Psychotic and motor symptoms were markedly improved. Since there was no change in cognitive functions, we added memantine at 5 mg p.o./d and gradually increased the dose to 20 mg p.o/d after five weeks. We continued risperidone and memantine for nearly six months. The patient did not show any progression of cognitive symptoms or motor abnormalities. We did not observe any psychotic symptoms.

**Key words:** Huntington's disease ■ psychiatry ■ cognitive symptoms

 From the Psychiatry Clinic (Cankurtaran; Ozalp; (Soygur, assistant professor/clinical director) and Neurology Clinic (Çakır), Ankara Oncology Training and Research Hospital, Ankara, Turkey. Send correspondence and reprint requests for *J Natl Med Assoc.* 2006;98:1353–1355 to: Dr. Ankara Onkoloji Egitim ve Arastırma Hastanesi, Psikiyatri Klinigi, (Ahmet Andicen Hastane Birimi), Mahmut Esat Bozkurt Caddesi, No 1, 06600 ,Kolej, Ankara, Turkey; phone: +90 312-4340990; fax: +90 312-4342213; e-mail: eylemcankurtaran@yahoo.com

## INTRODUCTION

Huntington's disease (HD) is a neuropsychiatric disorder with autosomal dominant inheritance. It is characterized by progressive movement disorders, and mental and behavioral abnormalities. It is generated by nucleotide triplet (CAG) repeats in the IT15 gene on the short arm of chromosome 4.[1] HD follows a relentlessly progressive course, resulting in death, usually 15–20 years after the onset of the disease. HD onset is defined by the beginning of motor symptoms, including tremor, balance difficulties and jerkiness.

Cognitive abnormalities usually begin simultaneously with movement abnormalities. The loss of mental flexibility and slowing of intellectual processes are some cognitive abnormalities that progress insidiously to profound dementia. Emotional abnormalities include psychosis, depression and manic-depressive disorder, as well as nearly universal changes in personality—mostly apathy and irritability.[2]

Here, we present a patient with HD whose psychotic symptoms, motor and cognitive abnormalities were controlled with risperidone and memantine treatment.

## CASE REPORT

A 32-year-old woman was admitted to the psychiatry clinic with increased involuntary movements that involved her face, body and limbs, gait and posture difficulties together with forgetfulness, pessimistic thoughts and changes in personality. She had little interest in the social contacts she used to have. Her complaints started eight years ago (at the age of 24) and worsened severely after she was 29 years old.

On admission to the hospital, her physical examination was normal, except for autonomic dysfunctions such as hypotension and gastric symptoms (diarrhea). Neurological assessment was made by a neurologist. The patient had postural instability and obvious choreic movements in her bilateral upper extremities and lower right extremity. She had involuntary facial movements, including frowning, blinking, clenching and puckering. Nocturnal myoclonus was present. We observed dysarthria, dysphagia, ideomotor apraxia and apraxia of palpebral movement, and difficulty in opening and closing both eyelids. She was oriented to people and place but disoriented to time. Her memory was poor regarding recent and remote events, when assessed with a free retrieval paradigm. Her mood was depressive, and she was apathetic. She exhibited auditory/ visual hallucinations and paranoid delusions.

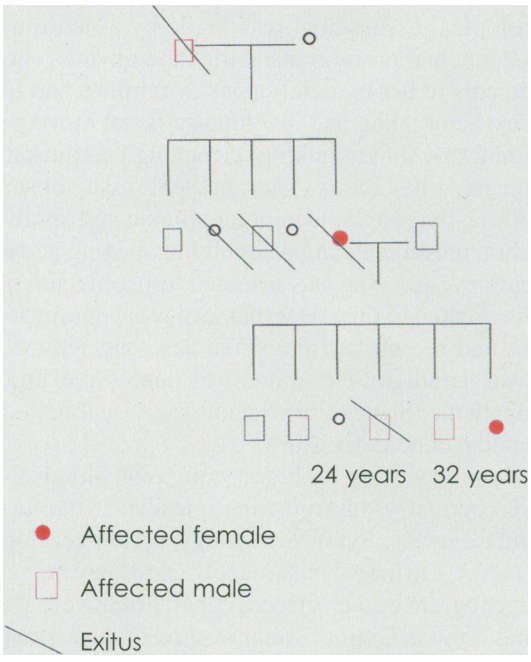
Laboratory tests included complete blood count, serum chemistry, thyroid function tests, vitamin-$B_{12}$ and folate levels. Syphilis serology, serum ceruloplasmin level, urinanalysis, electrocardiogram, chest roentgenogram and electroencephalogram were within normal limits. Cranial magnetic resonance imaging (MRI) showed slight cerebral cortical atrophy. DNA

analysis at the Genetic Department of Hacettepe University, School of Medicine identified an abnormal IT 15 allele with more than 36 CAG repeats (normal is <36 CAG repeats).

The patient had no history of medical illness other than HD. The patient's grandfather, mother and one brother had all died at 40–50 years of age, while they had been having the same symptoms as the patient. Also, one of her brothers had been having similar symptoms for the last two years. The pedigree is shown in Figure 1. She was diagnosed with HD together with clinical presentations of motor abnormalities, psychotic symptoms, cognitive deficits, personality changes, gradual deterioration of functioning, family history of probable HD and the result of genetic determination.

Subsequently, this patient was examined every two weeks and received a complete neurological and psychiatric evaluation besides administration of the Brief Psychiatric Rating Scale (BPRS), Abnormal Involuntary Movement Scale (AIMS) and Mini Mental Status Examination (MMSE). Upon admission, her score on the BPRS was 42, and her score on the AIMS was 34. A deficiency in intellectual functioning and deficits in memory were revealed, and the MMSE score was 16. We started risperidone at 2 mg p.o./d. Supportive treatment, such as family psychotherapy and nutritional guidance, were also applied. Two weeks later, improvements in gesture, gait and ability to use her hands (tying her shoelaces, eating, doing her laundry) were noted. AIMS score decreased to 26. Auditory/visual hallucinations and paranoid delusions had improved, and BPRS score was 31. Her cognitive performance was unchanged, as reflected in a MMSE score of 16. Six weeks later, her psychiatric symptoms had moderately decreased, BPRS score was 25, and her motor symptoms markedly decreased; AIMS score was 15. Since her psychotic symptoms had not decreased enough, her medication (risperidone) was increased to 4 mg p.o./d. After eight weeks, all the psychotic symptoms had disappeared. Since there was no change in cognitive function (the MMSE score was still 16), we added memantine at 5 mg p.o./d; one week later, we increased it to 10 mg p.o./d. At the 12th week, cognitive function abnormalities did not change, so we increased memantine to 20 mg p.o./d and decreased risperidone to 3 mg p.o./d. After four months, the patient was discharged from the hospital. We have continued to give her risperidone 3 mg p.o./d and memantine 20 mg p.o./d for six months. Her cognitive function has not changed; her score on the MMSE is still 16. No psychotic symptom has been observed, and there has been no progression of the motor abnormalities.

**Figure 1. The pedigree of the family**




## DISCUSSION

This case describes a patient with genetically confirmed HD whose psychiatric and neurological symptoms were improved by the risperidone. Also, the progression of cognitive symptoms of the patient have been most likely prevented by the memantine.

Few studies are available on the use of risperidone in HD patients for the abnormal involuntary movements.[3,4] Risperidone was well tolerated by this patient; the psychotic symptoms disappeared and motor symptoms improved markedly. In spite of aggravation of the Parkinsonian symptoms shown in some studies,[5] we did not observe any deterioration. It is unclear how risperidone may have beneficial effects in HD patients. Risperidone is a potent dopamine D2 receptor antagonist but also has low affinity for dopamine D4 receptor. The loss of D2-projection neurons, which are involved in the suppression of involuntary movements in the corpus striatum, is thought to be the pathophysiological mechanism of chorea of the HD.[2] It was also reported that risperidone showed some improvements in the cognitive functions, especially episodic memory, verbal fluency, vigilance and executive functioning for schizophrenic patients.[6]

It has long been suggested that N-metil D aspartate (NMDA)-receptor-mediated excitotoxicity contributes to cell death in the striatum for HD.[7] Some improvement on motor function and stability of the cognitive function were reported in studies with oral amantadine (a NMDA antagonist).[8] Memantine—the only uncompetitive NMDA receptor antagonist at the marketing—was thought to be beneficial for the cognitive problems of this patient and so was prescribed. A clinical study report showed that the progression of the Clinic Global Impression and HD Activities of Daily Living scores

were reduced during memantine treatment (up to 30 mg p.o./d) in 27 HD patients over two years' time in comparison with the reports of untreated HD patients.[9] The cognitive functions that deteriorate during the course of HD are mainly attention, object and space perception, and executive functions.[10] Our patient's cognitive functions measured by MMSE did not show any progression in six months' time. We propose that further studies are necessary to determine the usefulness of memantine and risperidone in the treatment of HD.

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